

REMARKS

In the Office Communication dated May 9, 2003, the Examiner states that Applicants reply filed on February 28, 2003 is not fully responsive to the Restriction Requirement issued December 31, 2002, because Applicants did not elect the particular sequence to which the relevant claims will be restricted. The Examiner requires Applicants to elect one of SEQ ID NOS: 1-5 in the context of the earlier elected group.

In the Restriction Requirement issued December 31, 2002, the Examiner requires Applicants to elect a single invention directed to a product or method drawn to one specific sequence. The Examiner states that this restriction to examination of a single sequence is due to the now very high and undue burden for examining more than one sequence which is caused by the continued exponential increase of size of the sequence databases to be searched for each sequence, resulting in a corresponding increase in computer search time and examiner time for reviewing the computer search results.

In response to the Office Communication and in connection with the prior election of Group II, Applicants further provisionally elect SEQ ID NO: 5 for continued prosecution. However, pursuant to 37 C.F.R. §§ 1.111 and 1.143, Applicants hereby traverse the Examiner's requirement for restriction with respect to the sequences and request reconsideration thereof in view of the following remarks.

Applicants respectfully submit that it is the unique recognition of the present invention that gene expression can be modulated by altering the number of sequence elements corresponding to pseudo-translation initiation sites, i.e., RUG or RTG (wherein R is A or G), within the 5' leader sequence upstream of the authentic translation initiation site. According to the present invention, elevated expression of a genetic sequence can be achieved by removing or destroying the RTG or

RUG triplets in the upstream sequence; and expression can be reduced by introducing or creating pseudo-translation initiation sites in the upstream sequence. Therefore, the present invention provides methods of modulating gene expression by removing or destroying one or more pseudo-translation initiation sites, or alternatively, by introducing or creating one or more pseudo-translation initiation sites, within the leader sequence of the gene. In addition, the present invention provides isolated nucleic acid molecules or genetic constructs which contain a predetermined number of pseudo-translation initiation sites such that a genetic sequence can be expressed at a predetermined level. Methods of modulating gene expression by employing various leader sequences, e.g., SEQ ID NOS: 1-5 or derivatives thereof, as well as nucleic acid molecules and genetic constructs containing a leader sequence (e.g., one of SEQ ID NOS: 1-5 or derivatives thereof), are clearly linked to each other as different aspects of a single invention.

Applicants respectfully submit that a determination to make the sequence restriction requirement final must evidence the patentable distinctness of the relevant methods or nucleic acid molecules relating to a specific sequence of SEQ ID NOS: 1-5, as presented by the Examiner.

In view of the foregoing comments, it is respectfully urged that the Examiner reconsider and withdraw the requirement for restriction and provide an action on the merits with respect to all the claims.

Respectfully submitted,



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